

## **Green, Enabling Technology Platforms for Drug Discovery, Nanotechnology Drug Delivery And Manufacturing Improvement**



**Trevor P. Castor - CEO**

### **About Aphios Corporation**

Aphios Corporation ([www.aphios.com](http://www.aphios.com)), a clinical-stage biotechnology company, is developing sustainable technologies and products from terrestrial plants, marine organisms and *homo sapiens* to combat chronic diseases and improve quality of life. Using advanced scientific and engineering principles, we have developed and patented green, enabling technology platforms for improving drug discovery and manufacturing, nanotechnology drug delivery, pathogen inactivation for viral vaccines and virus-free human plasma and biologics, and the sustainable manufacturing of biofuels and biochemicals from cellulosic biomass. Based on these platforms, we are developing quality-of-life medicines for health maintenance and disease prevention, and enhanced therapeutics for the treatment of certain cancers and supportive care, infectious diseases such as HIV/AIDS, and CNS disorders such as Alzheimer's disease.

**Interview conducted by: Lynn Fosse, Senior Editor, CEOCFO Magazine**

**CEOCFO: *Dr. Castor, Aphios is inspired by nature and enabled by science. What is the concept?***

**Dr. Castor:** This is an evolutionary concept. When we started the company, our vision was to develop safe and effective biologics and better ways to deliver them, basically deliver biologics orally. I spent some of my time looking at medicinal plants, and as the company evolved we realized that in order to solve some of the problems that we have with cancer and aging, such as Alzheimer's disease, we have to look to nature and marine organisms and terrestrial plants, which often live for thousands of years having learned to refine their DNA process of reproduction without cancerous mutation. Even though *homo sapiens* has been around for about 200,000 years, we are not as refined as some of the other parts of nature, but we can harness nature to improve our quality of life. That is the genesis of our evolutionary concept.

**CEOCFO: *What are you working on today?***

**Dr. Castor:** We are working on products that are very effective against nausea associated with cancer chemotherapy and other drug medications. It is in Phase III, and we are getting ready to do a pivotal Phase III trial before filing an NDA with the FDA. That product is from a plant, and we are working on a marine product that is effective against some of the problems associated with Alzheimer's disease. We have done an exploratory clinical trial with good results, and have done a large amount of research in animal studies with Alzheimer's disease transgenic mice that are quite effective. We are getting ready to file an IND with the FDA to continue our research in that area. Our third clinical product is on HIV latency. We have an IND (which is called an IMPD in Spain) that is filed and approved, and we are getting ready to do a clinical trial on this product. HIV latency is a problem for millions of HIV patients who are on ART therapy. If they are removed from therapy, the virus rebounds. They are really stuck with a very toxic and expensive therapeutic regimen, so our goal is to develop an HIV cure by getting rid of HIV from latent reservoirs and then using ART to eradicate HIV from a patient's body so they can become disease-free, cured of HIV.

**CEOCFO: *How have you decided where to focus?***

**Dr. Castor:** We started-off by looking at how biologics can be manufactured and delivered safely. We started by researching biosynthetic insulin, because that was the first recombinant product approved by the FDA. Today, we have come almost full circle in that we just had a US patent issued to improve the oral delivery of insulin to improve the quality of life in diabetics. We initially focused on developing several enabling technology platforms and then focused on therapeutic targets that presented themselves to us in different ways. For example, my mother-in-law became afflicted with Alzheimer's disease at quite an early age. At 60, she was a university professor who often got lost in the university system because she went to the wrong classrooms. Eventually, she died because of the disease that was very chronic and debilitating, which gave me a passion for addressing that issue. It turned out that one of the drugs we were working on has an impact on this particular disease. On HIV latency, from the very start of the company, we asked what we could

do to arrest this epidemic and pandemic of HIV around the world. We looked at ways to inactivate the virus, which is a way to clear viruses from human biologics and recombinant therapeutics to prevent blood transfusion of HIV and other viruses. Of course, therapies evolved and developed over the last few years for HIV, but they left behind the inability of the virus to be cleared totally from the body. Based on our research on antivirals from marine sources, we discovered a compound which was quite effective in releasing HIV from its hidden sources, and that is part of the development history of our product for HIV latency.

**CEOCFO: *What is the general feeling in the medical community today about biologics?***

**Dr. Castor:** I believe that biologics are a very progressive way of approaching therapeutics. If we can harness the enzymes and proteins in our body to address certain diseases and genetic deficiencies, then we have a great potential source of therapeutic interventions. When you look at it that way, it is really the end solution of how we can manage health care, but there are some challenges. How do we deliver these biologics back into our bodies? They are very complex proteins, and the only way we can do this intravenously or subcutaneously and orally is a challenge that we are addressing. Biologics are, however, not perfect drugs because every drug has toxicity, which is dependent on the dosing level. I believe that the medical community has made a great deal of progress, although biologics are still very complicated and challenging.

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**- Trevor P. Castor**

**CEOCFO: *What is the science behind your Phase III product?***

**Dr. Castor:** Our Phase III product is based on ginger, which has been historically used for combatting diseases of the stomach and intestinal system, but there was no standardized way of doing it. There was no identification of active ingredients, so we standardized it based on chemistry of some of the leading bioactive components. When we went into the clinic, we did a large-scale clinical trial of 644 patients. We did not know if it was going to work, but it was a very well designed, randomized, placebo controlled, multi-arm trial. It was successful. Since then, we have gone back into the labs to look at why it was successful. It is difficult to define success with nausea because there are no good in vitro or animal models. You cannot ask ferrets or mice if they are experiencing nausea. However, we developed an assay based on stomach lining skin cells that have demonstrated our product works by a serotonin-based mechanism. Nausea is associated with a transmission between the stomach and the mind where the stomach is telling the mind that it has to respond to an invasive species and the mind then instructs the stomach to get rid of that species. This same type of connection with mind and body works with motion sickness, pregnancy-related nausea and vomiting, and post-operative nausea and vomiting. We believe that our product is a serotonin receptor antagonist.

**CEOCFO: *Your site indicates you offer products for sale. What else is happening at Aphios?***

**Dr. Castor:** A few years ago, we decided that part of what we do is to improve quality of life for healthy people apart from combatting chronic diseases for sick people. You hear about many healthy people who can do with a little bit of therapeutic help without having to do go through a highly regulated FDA process, so we recently launched a health and wellness center where we can sell products that are manufactured to the strict controls that pharmaceuticals are, but are not going through the FDA-regulated process. We call them dietary supplements or quality-of-life medicines. We do sell those online, and we also sell research chemicals to research institutions all over the world through distributors such as Sigma-Aldrich, Enzo Biomol and Tocris BioSciences in England, KeraFast and a number of other research institutions or marketing and distribution companies.

**CEOCFO: *Development and commercialization are always costly. Do your products help mitigate the cost? Are they just more ancillary?***

**Dr. Castor:** Our health and wellness products will help mitigate the cost of therapeutics. If a well patient can maintain health by using quality of life medicines, it reduces the cost of going to the hospital or to medical interventions. Our health and wellness products are designed to keep the patient healthy, and that will mitigate the future cost of being unhealthy. Of course, if we are successful in modifying or curing Alzheimer’s disease and HIV/AIDS, our products will have a significant impact on mitigating healthcare costs while improving quality of life.

**CEOCFO: *Are you funded for the developments you would like to do and the efforts you would like to make?***

**Dr. Castor:** We are self-funded based on my initial investment into the company, and through collaborations with pharmaceutical companies and biotechnology companies, National Institutes of Health grants, and contracts with the National Cancer Institute as well as product sales. Going forward, because it is so capital-intensive to conduct rigorous clinical trials, we are currently raising a mezzanine round of financing to finish Phase III clinical trials of our anti-nausea

drug, to start off the clinical trial of our Alzheimer's disease lead APH-1104 and to continue the development of our HIV latency compound in Spain, which is APH-0812.

**CEOCFO: *Why Spain?***

**Dr. Castor:** We have an HIV/AIDS physician who will conduct the clinical investigation in Madrid, and we have collaborators in Cordoba who have worked with us over the last five or six years on this particular compound for this particular application.

**CEOCFO: *With so much going on, how do you keep on track? How do you as CEO keep it all together in each area?***

**Dr. Castor:** There is a commonality in all the areas that we work. We are instrumental in discovering the compounds that we work with, we manufacture them and we have developed the formulations for them. Then, there is a common thread that they are not diverse in terms of mechanisms of action. We tend to keep buckets of focus in different areas, and one of the strategies that we have is instead of financing the company as a whole, we are willing to finance individual projects and create LLCs that will be focus buckets in order to better manage the financial aspect and the science efforts.

**CEOCFO: *There are so many products in the market. How will you get attention?***

**Dr. Castor:** We believe that we get attention by differentiating our product line and making sure that they are effective, high quality and safe. For example, there are no products in the marketplace that really impact nausea for cancer patients or other patients effectively. That would be a single impact, which would differentiate us from most products such as Aloxi, which is a 5-HT3 serotonin antagonist and Emend, which is a NK-1 antagonist. These are anti-emetic drugs, but they really do not impact nausea. In a pivotal Phase III clinical trial Emend did impact vomiting, but not nausea, so that is a niche differentiation from that particular product. With Alzheimer's, of course, there are no products in the marketplace that work today. Pfizer's product Aricept works as a Band-Aid. It is not really an effective treatment or cure to Alzheimer's disease. Most of the products in the Alzheimer's disease market are Band-Aids. Over the last few years, new approaches being developed have been enzyme inhibitors, gamma secretase and beta secretase, which have proven to be either neurotoxic or kidney toxic and have not passed clinical trials. Our product on the other hand up-regulates a key enzyme, alpha-secretase, which will clear the toxic amyloid precursor protein from the brain. Therefore, we believe it has a set of effects that differentiate it from either the gamma or beta secretase inhibitors that are being evaluated, or the current drugs in the marketplace that are not effective.

**CEOCFO: *Would you tell us about community involvement and giving back at Aphios?***

**Dr. Castor:** We really believe our community giving back starts with our internship programs. We have always had active internship programs working with undergraduates. What I like about our program and have seen in the graduates who have come in without any idea what to do after graduation, a significant amount of them have gone on to do research at major universities and have finished advanced degrees, PhDs and MDs. That is one aspect of giving back that we have done. Another aspect is being a peer reviewer for the National Institutes of Health, which I have done that over the last 15 years. We also contribute to causes which are near and dear to our hearts, and that encapsulates what we do in terms of community give back.

**CEOCFO: *What are the next steps? What will be different two years from now?***

**Dr. Castor:** Hopefully, two years from now we will have made progress in our clinical development of the three drugs in our pipeline and we will have continued to expand our health and wellness program. From there, we will be able to give back to communities. Interestingly enough, we support a program in Ghana for malaria prevention in infants and babies in the first 90 days of life, which is really an on-the-ground program that we are involved in. I believe we can do much more in terms of this kind of effort and be more financially secure as a company.

**CEOCFO: *Put it all together for our readers. Why Aphios?***

**Dr. Castor:** I believe that since our existence, we have evolved into developing sustainable solutions to improve quality of life and combat chronic diseases. We have done so by harnessing the power of medicinal plants and marine organisms and homo sapiens. We have developed many enabling technologies to improve the way drugs are discovered, manufactured and delivered, and how to keep them safe from pathogens. From such platforms, we are developing several therapeutic options for both healthy and sick people. Apart from the three lead therapeutic areas that we are involved in – nausea, Alzheimer's disease and HIV latency – we have a large suite of preclinical drugs in various stages of development, some with collaborators such as a lead candidate for Multiple Sclerosis and Parkinson's disease.

**CEOCFO: *Final thoughts?***

**Dr. Castor:** I believe our growth and progress will only be limited by the interest that we can generate and the capital that we can raise because drug development is a very long, arduous and capital-intensive roadway, but it is also very rewarding. Our general philosophy is to do 'good'. When I say do 'good', I mean do 'good' in improving health care. If we do 'good' in improving health care, we will do well, and we will do well for both our investors and our strategic corporate partners.

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**BIO:** Dr. Trevor P. Castor, Ph.D., President and Chief Executive Officer, has over 30 years of diversified business experience ranging from management, marketing and finance to technology and business development in the energy, environmental and biopharmaceutical industries. He has had bottom-line experience with several high-tech startups. Dr. Castor graduated from the University of California, Berkeley, with a Ph.D. in Mechanical Engineering and a Master of Science degree in Chemical Engineering. He graduated summa cum laude with a Bachelor of Science degree in Chemical Engineering from the University of Toronto, Toronto, Canada. He studied Business Administration at St. Mary's College, Brooklyn, NY, and Management, Marketing and Finance at the Harvard University Extension Program, Cambridge, MA. He is the primary author of 43 issued US and international patents and 15 pending patents. Dr. Castor has collaborated with and consulted to several multinational companies including Baxter Healthcare, Bayer AG, Bristol-Myers Squibb, Eli Lilly, General Electric, Novartis AG and the Gillette Company, and financial institutions such as the Bank of New England and the New England Life Insurance Company.

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